A collaborative pathway to establish credible practice of modeling and simulation in knee biomechanics in conformance with community recommendations

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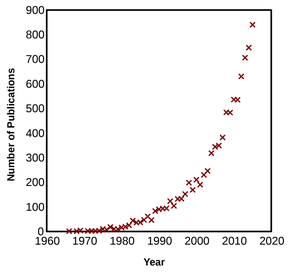
BACKGROUND

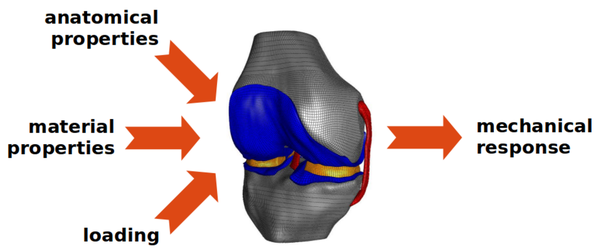
Computational modeling and simulation (M&S) has become a routine strategy in knee biomechanics for

- scientific knowledge
  joint and tissue function
  impact of pathology
  injury mechanisms
  surgical interventions
- clinical guidance
  osteoarthritis
  meniscal tears
  ligament injuries
  joint pain
  rehabilitation

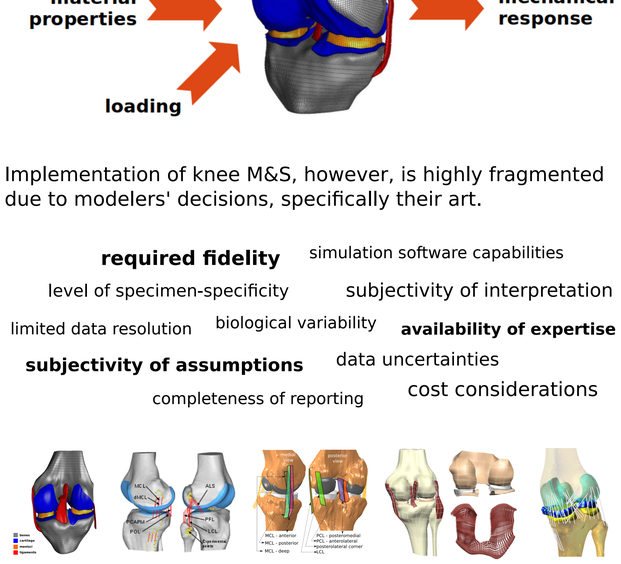
PubMed Search
"knee AND (model OR simulation)"
Total Citations = **9,687** (1960-2015)



Abstraction and fundamental components of knee M&S to explore biomechanical function are unified.



Implementation of knee M&S, however, is highly fragmented due to modelers' decisions, specifically their art.



*Do the **predictions** of natural knee biomechanics **depend** on **modeling decisions** of separate development teams **when** the target simulation scenarios and the **source data** to build models remain the **same**?*

Our multi-team collaboration aims to understand the **"art"** of M&S in knee biomechanics:

- To quantify the influence of variations in M&S workflows on the reproducibility of joint level predictions
- To quantify the influence of variations in M&S workflows on the reproducibility of tissue level predictions

This document establishes the correspondence between the design of our **reproducibility study on knee M&S** and the broad **guidance** from biomedical community **on credible practice of M&S**.

- To summarize our study design to understand, document, and review multiple M&S workflows in knee biomechanics.
- To establish mapping of the components of our knee M&S project to Ten "Not" So Simple Rules of Credible Practice of M&S in healthcare.

TEN "NOT SO" SIMPLE RULES

By Committee on Credible Practice of Modeling & Simulation in Healthcare.
To learn more about the Committee, refer to https://simtk.org/plugins/moinmoin/cpms/.

1. *Define context clearly* — Plan and develop the M&S activity with clear definition of the intended purpose or context accommodating end-users needs.
2. *Use appropriate data* — Use data relevant to the M&S activity, which can ideally be traced back to the source.
3. *Evaluate within context* — Evaluate the M&S activity through verification & validation, uncertainty quantification, and sensitivity analysis faithful to the context/purpose/scope of the M&S efforts, with clear and a-priori definition of evaluation metrics and including test cases.
4. *List limitations explicitly* — Provide an explicit disclaimer on the limitations of the M&S to indicate under what conditions or applications the M&S may or may not be relied on.
5. *Use version control* — Implement a version control system to trace the time history of the M&S activities, including delineation of contributors' efforts.
6. *Document adequately* — Document all M&S activities, including simulation code, model markup, scope and intended use of M&S activities, users' and developers' guides.
7. *Disseminate broadly* — Disseminate appropriate components of M&S activities, including simulation software, models, simulation scenarios and results.
8. *Get independent reviews* — Have the M&S activity reviewed by independent third-party users and developers, essentially by any interested member of the community.
9. *Test competing implementations* — Use competition of multiple implementations to check the conclusions of different implementations of the M&S processes against each other.
10. *Conform to standards* — Adopt and promote generally applicable and discipline specific operating procedures, guidelines, and standards accepted as best practices.

For additional details, refer to Erdemir, A., Mulugeta, L. and Lytton, W. W. Ten "not so" simple rules for credible practice of modeling and simulation in healthcare: a multidisciplinary committee perspective, 2015 Biomedical Engineering Society / Food and Drug Administration Frontiers in Medical Devices Conference: Innovations in Modeling and Simulation, May 18-20, 2015, Washington, DC.

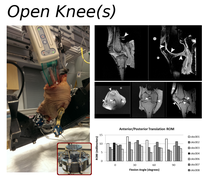
DATA

Reuse of existing data on knee anatomy and mechanics

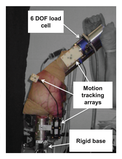
1 knee from Open Knee(s)
- 8 cadaver knees from 8 donors
- Medical imaging (MRI)
- Joint kinematics-kinetics
- Tissue testing

1 knee from Natural Knee Data
- 7 cadaver knees from 5 donors
- Medical imaging (CT, MRI)
- Joint kinematics-kinetics

Open Knee(s)



Natural Knee Data



M&S PHASE: CALIBRATION

Start with

Initial specimen-specific knee model
Specimen-specific joint kinematics-kinetics
- laxity datasets
Literature

Deliver

Calibrated specimen-specific knee model
Calibration fit error (before & after)
Loading and boundary conditions
Changes in anatomical representation
Changes in tissue representation

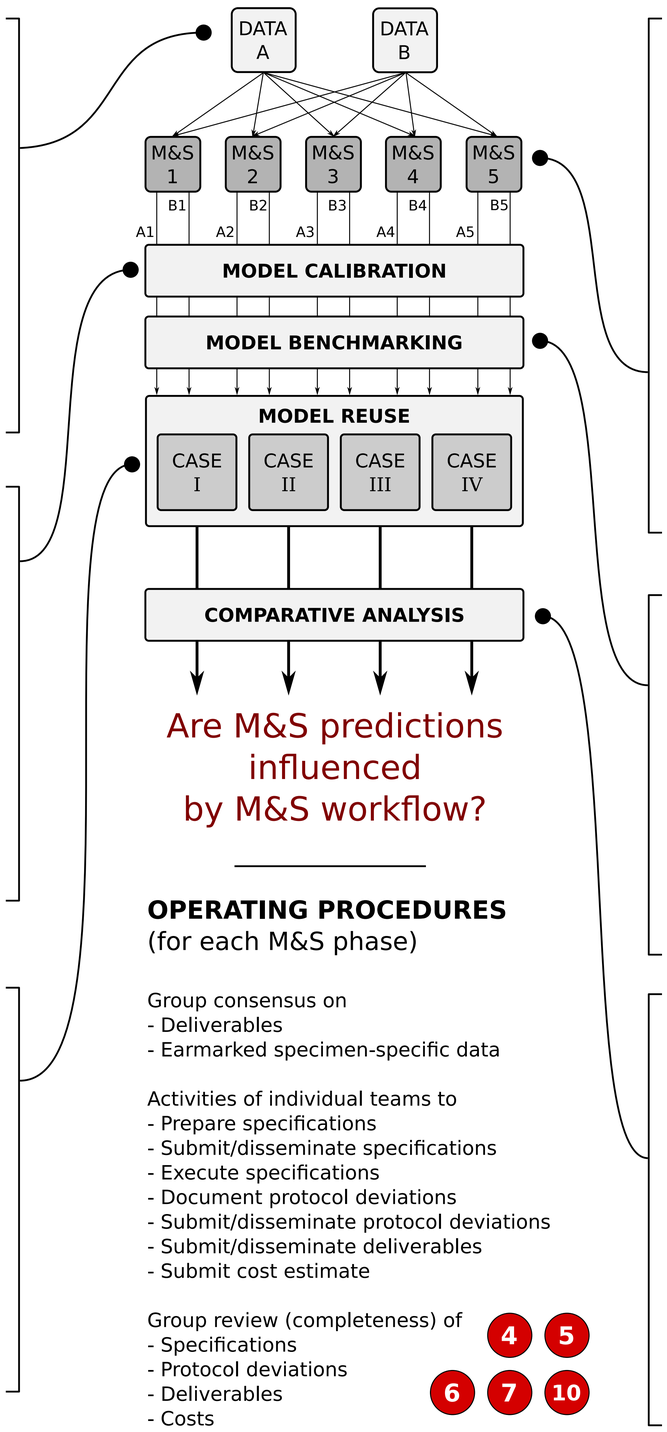
M&S PHASE: REUSE

Start with

Benchmarked specimen-specific knee model
Simulation cases
- Passive flexion
- Pivot shift
- Weight-bearing standing (x-ray)
- Sit-to-stand motion

Deliver

Loading and boundary conditions
Joint mechanics predictions
Tissue mechanics predictions



OPERATING PROCEDURES
(for each M&S phase)

Group consensus on
- Deliverables
- Earmarked specimen-specific data

Activities of individual teams to
- Prepare specifications
- Submit/disseminate specifications
- Execute specifications
- Document protocol deviations
- Submit/disseminate protocol deviations
- Submit/disseminate deliverables
- Submit cost estimate

Group review (completeness) of
- Specifications
- Protocol deviations
- Deliverables
- Costs

M&S PHASE: DEVELOPMENT

Start with

Specimen-specific medial imaging datasets
Literature

Deliver

Initial specimen-specific knee model

Representation of anatomy
- Segmentation
- Geometry
- Mesh

Representation of tissue behavior
- Constitutive models
- Tissue stress-strain response
- Tissue bulk response

5 M&S teams

Cleveland Clinic
University of Denver
Cleveland State University
Auckland Bioengineering Institute, The University of Auckland, New Zealand
Hospital for Special Surgery

M&S PHASE: BENCHMARKING

Start with

Calibrated specimen-specific knee model
Specimen-specific joint kinematics-kinetics
- combined loading datasets
- datasets from resected joint

Deliver

Benchmarked specimen-specific knee model
Benchmark error
Loading and boundary conditions

THIRD-PARTY REVIEW & COMPARISON

Deliverables
- Models
- Model components
- Simulation results

Modeling & simulation workflows
- Specifications
- Protocol deviations
- Reporting

Predictive capacity
- Calibration results
- Benchmarking results

Model reuse credibility and criticality assessment

collaboration with US FDA for independent review

POSTER GOALS

STUDY DESIGN ON "ART" OF MODELING

From project Reproducibility in Simulation-Based Prediction of Natural Knee Mechanics.
For a copy of the grant proposal, refer to https://simtk.org/svn/kneehub/doc/grant_resubmission.pdf.

Project Title: Reproducibility in simulation-based prediction of natural knee mechanics
Project Funding: NIBIB, NIH (R01EB024573; PI: Erdemir)
Project Website: https://simtk.org/projects/kneehub
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